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Original Research Paper

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A RARE CASE OF BENIGN RECURRENT INTRAHEPATIC CHOLESTASIS (BRIC) PRESENTING AS UNEXPLAINED CHOLESTASIS JAUNDICE

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ABSTRACT

Introduction: Benign Recurrent Intrahepatic Cholestasis (BRIC) is a very rare autosomal recessive disorder characterized by episodes of recurrent cholestatic jaundice manifested as pruritus, anorexia, fatigue, steatorrhea followed by complete resolution. Inheritance follows an autosomal recessive pattern with mutation in both alleles of ATP8B1 (BRIC1) or ABCB11 (BRIC2). It causes cholestasis by impairing the function of the bile salt export pump. The index episode usually occurs in the first two decades of life. Episodes can be spontaneous or triggered by infections or pregnancy and can last from weeks to months Recognition of BRIC is important as it can lead to delayed or no diagnosis, also it is under recognized and challenging. **Case Report:** A 23 year old female patient was admitted with a 8 Weeks history of jaundice. Jaundice was accompanied with symptoms of pruritis high coloured urine and clay coloured stools, which started during the last week of third trimester Of her third pregnancy and persisting even after the delivery There was no history of accompanying pain abdomen, drug exposure, fever, nausea and vomiting or diarrhoea. She had had 3 similar episodes in the past at the ages of 13,18 and 21 years The first episode had lasted for about 2 weeks, second episode for 10. Weeks after her first pregnancy and third Episode lasted for 6 weeks. After her second pregnancy. All the episodes subsided Spontaneously without any treatment She reported history of similar episodes in her elder sister as well She had no history of viral hepatitis food or drug allergies alcohol and tobacco abuse. On examination, she is conscious and coherent, poorly built and nourished with a BMI of 17.5 Pulse rate-72/min, blood pressure is 110/80 mmhg in the right upper limb in the supine position. Icterus present and scratch marks are present all over the body No Kayser-Fleischer ring, cyanosis, clubbing, pedal edema or lymphadenopathy. No signs of liver cell failure. No organomegly or ascites on palpation of abdomen and bowel sounds heard. The respiratory, cardiovascular and central nervous system **Discussion:** BRIC (Benign Recurrent Intrahepatic Cholestasis), first described in 1959 has since been reported to occur worldwide. Till date very few cases of BRIC have been reported, which may be due to the rarity of the condition compounded by under-recognition by clinicians. Inheritance follows an autosomal recessive pattern with mutations in both alleles of ATP8B1 (BRIC1) or ABCB11 (BRIC2). Both mutations cause cholestasis by impairing the function of the bile salt export pump (BSEP), which actively transports bile into canaliculi. Despite being a genetic disease, most cases are sporadic. The first episode usually occurs in the first two decades of life. Episodes can last from weeks to months and can be of varying severity. **Conclusion:** Benign recurrent intrahepatic cholestasis should be considered in the differential Diagnosis of recurrent intrahepatic cholestasis in young aged patients without signs of liver cell failure. It is a rare inherited cholestatic disorder with a good prognosis. Early diagnosis and confirmation with liver biopsy help to prevent other expensive Investigations. Patients can be managed symptomatically and followed up.

KEYWORDS :

INTRODUCTION

Benign Recurrent Intrahepatic Cholestasis (BRIC) is a very rare autosomal recessive disorder characterized by episodes of recurrent cholestatic jaundice manifested as pruritus, anorexia, fatigue, steatorrhea followed by complete remplution. Inheritance follows an autosomal recessive pattern with mutation in both alleles of ATP8B1 (BRIC1) or ABCB11 (BRIC2).

It causes cholestasis by impairing the function of the bile salt export pump. The index episode usually occurs in the first two decades of life. Episodes can be spontaneous or triggered by infections or pregnancy and can last from weeks to months Recognition of BRIC is important as it can lead to delayed or no diagnosis, also it is underrecognized and challenging.

Diagnosis is based on a compatible clinical presentation, laboratory parameters and histology with exclusion of other causes of cholestasis Despite being recurrent, BRIC does not progress to advanced liver disease. We intend to report this case due to rarity of this disease in India

Case Report

A 23 year old female patient was admitted with a 8weeks history of jaundice. jaundice was accompanied with symptoms of pruritis high coloured urine and clay coloured stools, which started during the last week of third trimester Of her third pregnancy and persisting even after the delivery.

There was no history of accompanying pain abdomen, drug exposure, fever, nausea and vomiting or diarrhoea. She had had 3 similar episodes in the past at the ages of 13,18 and 21 years The first episode had lasted for about 2 weeks, second episode for 10 weeks after her first pregnancy and third Episode lasted for 6 weeks after her second pregnancy.

All the episodes subsided Spontaneously without any treatment She reported history of similar episodes in her elder sister as well She had no history of viral hepatitis food or drug allergies, alcohol and tobacco abuse. On examination, she is conscious and coherent, poorly built and nourished with a BMI of 17.5 Pulse rate-72/min, blood pressure is 110/80 mmhg in the right upper limb in the supine position. Icterus present and scratch marks are present all over the body. No Kayser-Fleischer ring, cyanosis, clubbing, pedalled or lymphadenopathy. No signs of liver cell failure. No. organomegly or ascites on palpation of abdomen and bowel sounds heard. The respiratory, cardiovascular and central nervous system was unremarkable.

Investigation

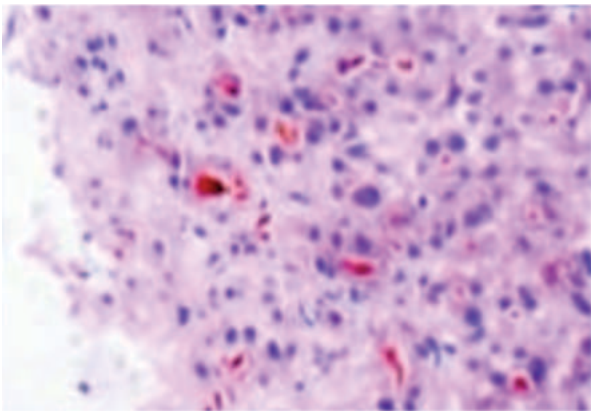
Viral markers for hepatitis A,B,C,E ; HIV 1 & 2; EBV and CMV were negative. Workups for autoimmune hepatitis and Wilson's disease were negative Antinuclear, anti-smooth

muscle,anti-mitochondrial,anti-LKM1 antibodies are negative Ultrasonography showed lived span of 11.5cm with uniform echo-pattern with no Evidence of local or diffuse pathology and normal intra and extrahepatic biliary radicle Upper gastrointestinal scopy showed normal mucosa without varices Magnetic resonance cholangiopancreatography showed normal intrahepatic and extrahepatic Biliary radicle with no evidence of stone in the common bile duct.

Liver biopsy showed a maintained lobular architecture comprised of hepatocytes showing scattered intrahepatocytic Cholestasis and focal lobular inflammation, bile canaliculi showing prominent intracanalicular cholestasis comprised dark Brown coarse bile pigments, portal tracts show minimal lymphocytic infiltrates and no portal fibrosis, significant inflammation or nodule formation.

Diagnostic Criteria for BRIC

At least two attacks of jaundice separated by a symptom-free interval lasting several months to years Laboratory values consistent with intrahepatic cholestasis GGT either normal or only minimally elevated. Severe pruntus secondary to cholestasis Liver histology demonstrating centricbular cholestasis Normal intra- and extrahepatic bile ducts by cholangiography Absence of factors known to be associated with cholestasis



Canalicular Cholestasis And Focal Degeneration

Hb	Rbc	Platelet	TLC	Urea	Creat	Sodium	Potassium	INR	Amylase/ lipase
14.2	5.21	279	8.7	26	0.76	135	3.90	0.91	28/23

	Total bilirubin	Direct bilirubin	ALP	GGT	ALT	AST
DAY 1	8.2	6.1	388	15.2	415	205
DAY 7	12.4	9.8	421	14.8	354	106
DAY 14	14.6	12.2	510	13.5	156	88
DAY 21	18.0	16.5	615	12	80	60
DAY 30	17.4	15.2	500	11.6	48	32
DAY 45	12.24	9.6	480	10.2	38	22
DAY 60	7.2	5.8	350	9.6	36	20
DAY 90	1.6	0.8	86	9	28	15

DISCUSSION

- BRIC (Benign Recurrent Intrahepatic Cholestasis), first described in 1959 has since been reported to occur worldwide. Till date very few cases of BRIC have been reported, which may be due to the rarity of the condition compounded by under-recognition by clinicians.
- Inheritance follows an autosomal recessive pattern with mutations in both alleles of ATP8B1 (BRIC1) or ABCB11 (BRIC2). Both mutations cause cholestasis by impairing the function of the bile salt export pump (BSEP), which actively transports bile into canaliculi.
- Despite being a genetic disease, most cases are sporadic. The first episode usually occurs in the first two decades of life. Episodes can last from weeks to months and can be of varying severity.
- Diagnosis in our case was based on the past episodes of jaundice, present clinical features, laboratory parameters and liver biopsy findings as proposed by Luketic and Shiffman for the diagnosis of BRIC.
- This is a self- limiting disease with no residual damage and treatment is aimed at relieving symptoms and shortening of episodes.
- High dose fat-soluble vitamins should be supplemented to prevent deficiency during prolonged episodes.Bile acid sequestrants such as cholestyramine and ursodeoxy-cholic acid may reduce pruritus but not the duration of episodes.
- Rifampicin, plasmapheresis have shown to relieve symptoms and shorten episodes. The effectiveness of Rifampicin is related to its enzyme-inducing effects, Endoscopic nasobilia drainage is an effective treatment option in patients refractory to standard therapy.
- In between episodes, patients remain totally devoid of symptoms for periods ranging from months to years. Triggers, include stress, pregnancy, respiratory and gastrointestinal infections.

CONCLUSION

Benign recurrent intrahepatic cholestasis should be considered in the differential diagnosis of recurrent intrahepatic cholestasis in young aged patients without signs of liver cell failure. It is a rare inherited cholestatic disorder with a good prognosis. Early diagnosis and confirmation with liver biopsy help to prevent other expensive investigations. Patients can be managed symptomatically and followed up.

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